

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 Apr 08 "Ask CAS" for self-help around the clock
NEWS 3 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4 Apr 09 ZDB will be removed from STN
NEWS 5 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 9 Jun 03 New e-mail delivery for search results now available
NEWS 10 Jun 10 MEDLINE Reload
NEWS 11 Jun 10 PCTFULL has been reloaded
NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;
 saved answer sets no longer valid
NEWS 14 Jul 29 Enhanced polymer searching in REGISTRY
NEWS 15 Jul 30 NETFIRST to be removed from STN
NEWS 16 Aug 08 CANCERLIT reload
NEWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18 Aug 08 NTIS has been reloaded and enhanced
NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)
 now available on STN
NEWS 20 Aug 19 IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced
NEWS 23 Sep 03 JAPIO has been reloaded and enhanced

NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,
 CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
 AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS STN Operating Hours Plus Help Desk Availability
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NEWS WWW CAS World Wide Web Site (general information)

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 19:34:46 ON 08 SEP 2002

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 19:34:58 ON 08 SEP 2002

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STRUCTURE FILE UPDATES: 6 SEP 2002 HIGHEST RN 447682-31-7
 DICTIONARY FILE UPDATES: 6 SEP 2002 HIGHEST RN 447682-31-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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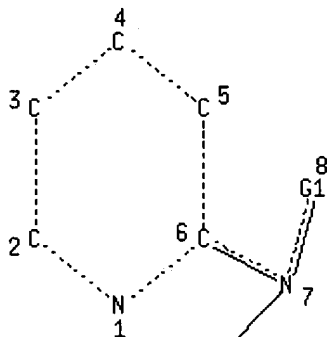
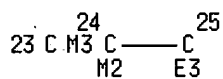
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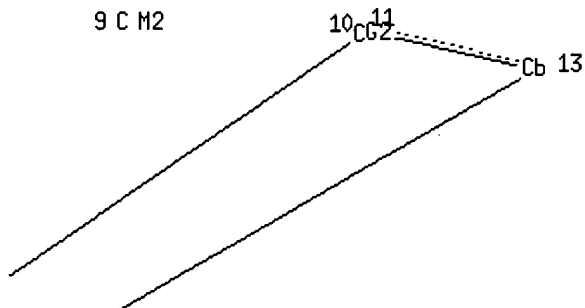
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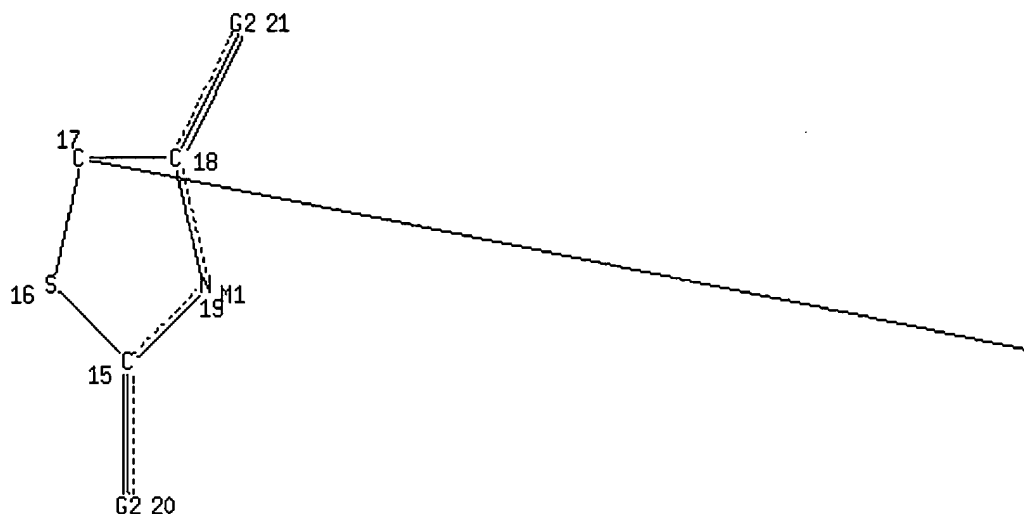


Page 1-C

9 C M2



Page 1-D



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Page 2-B

Page 2-C

14 C M2

Page 2-D
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 VAR G2=26/27
 REP G19=(1-2) 14-17 14-13
 REP G20=(1-2) 9-7 9-11

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GGCAT IS MCY LOC UNS AT 13
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS E6 C AT 13

GRAPH ATTRIBUTES:

RSPEC I
NUMBER OF NODES IS 27

STEREO ATTRIBUTES: NONE

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SAMPLE SEARCH INITIATED 19:41:55 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 4 TO ITERATE

100.0% PROCESSED 4 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 4 TO 200
PROJECTED ANSWERS: 2 TO 124

L2 2 SEA SSS SAM L1

=> s 11 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 139.90 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
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FULL SCREEN SEARCH COMPLETED - 113 TO ITERATE

100.0% PROCESSED 113 ITERATIONS 49 ANSWERS
SEARCH TIME: 00.00.03

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=> file hcaplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

144.46

144.67

FILE 'HCAPLUS' ENTERED AT 19:42:19 ON 08 SEP 2002

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FILE COVERS 1907 - 8 Sep 2002 VOL 137 ISS 11

FILE LAST UPDATED: 6 Sep 2002 (20020906/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s 13

L4 477 L3

=> s 14 and pd < june 1999

19625192 PD < JUNE 1999

(PD<19990600)

L5 153 L4 AND PD < JUNE 1999

=> s 15 and blacker, p?/au

4 BLACKER, P?/AU

L6 0 L5 AND BLACKER, P?/AU

=> s 14 and blackier, p?/au

0 BLACKIER, P?/AU

L7 0 L4 AND BLACKIER, P?/AU

=> s 14 and polymorph

5377 POLYMORPH

6362 POLYMORPHS

9607 POLYMORPH

(POLYMORPH OR POLYMORPHS)

L8 3 L4 AND POLYMORPH

=> d 18, ibib abs fhitr, 1-3

L8 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS

Full
Text

Citing
References

ACCESSION NUMBER: 2000:772629 HCAPLUS

DOCUMENT NUMBER: 133:340315

TITLE: Therapeutic action and properties of a polymorphic form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt

INVENTOR(S): Blackler, Paul David James; Browne, Christine Marie; Coakley, Timothy G.; Giles, Robert Gordon; Morrissey, Gillian

PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK; SmithKline Beecham (Cork) Limited

SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

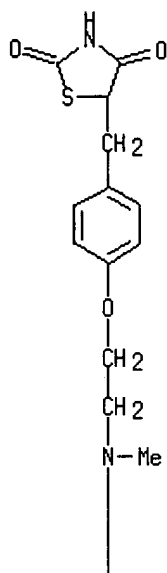
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

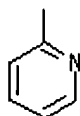
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064896	A1	20001102	WO 2000-GB1520	20000419
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1173435	A1	20020123	EP 2000-920892	20000419
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BR 2000009932	A	20020409	BR 2000-9932	20000419
NO 2001005147	A	20011217	NO 2001-5147	20011022
<u>PRIORITY APPLN. INFO.:</u>				
			GB 1999-9473	A 19990423
			GB 1999-12196	A 19990525
			WO 2000-GB1520	W 20000419
AB	A polymorphic form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2, 4-dione, maleic acid salt (the " Polymorph ") characterized in that it provides: (i) an IR spectrum contg. peaks at 1763, 912, 856 and 709 cm ⁻¹ ; and/or (ii) a Raman spectrum contg. peaks at 1762, 1284, 912 and 888 cm ⁻¹ ; and/or (iii) a solid-state ¹³ C NMR spectrum contg. peaks at 111.0, 113.6, 119.8, 129.1, 130.9, 131.8, 134.7, 138.7, 146.5, 152.7, 157.5, 169.5, 171.0, 178.7 ppm; and/or (iv) an x-ray powder diffraction (XRPD) pattern which gives calcd. lattice spacings at 5.87, 5.30, 4.69, 4.09, 3.88, 3.61, 3.53 and 3.46 Angstroms; a process for prepg. such a compd., a pharmaceutical compn. contg. such a compd. and the use of such a compd. in medicine.			
IT	<u>155141-29-0</u>			
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)			
	(antidiabetic action and properties of polymorphic form of			
	[[(N-methyl-N-(pyridyl)amino)ethoxy]benzyl]thiazolidinedione maleate)			
RN	<u>155141-29-0</u> HCAPLUS			
CN	2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)			
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CRN	<u>122320-73-4</u>			
CMF	C18 H19 N3 O3 S			

PAGE 1-A



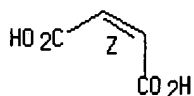
PAGE 2-A



CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

Double bond geometry as shown.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 2000:772627 HCAPLUS
DOCUMENT NUMBER: 133:340314
TITLE: Therapeutic action and properties of a polymorphic form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt
INVENTOR(S): Blackler, Paul David James; Giles, Robert Gordon; Moore, Stephen; Sasse, Michael John
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064893	A2	20001102	WO 2000-GB1522	20000419
WO 2000064893	A3	20010125		
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1175418	A2	20020130	EP 2000-922793	20000419
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BR 2000009935	A	20020416	BR 2000-9935	20000419
NO 2001005148	A	20011217	NO 2001-5148	20011022

PRIORITY APPLN. INFO.:

GB 1999-9471	A	19990423
GB 1999-12195	A	19990525
WO 2000-GB1522	W	20000419

AB A polymorphic form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt (the "**Polymorph**") characterized in that it provides: (i) an infra red spectrum contg. peaks at 1752, 1546, 1154, 621, and 602 cm^{-1} ; and/or (ii) a Raman spectrum contg. peaks at 1751, 1243 and 602 cm^{-1} ; and/or (iii) a solid-state NMR spectrum contg. peaks at 111.9, 114.8, 119.6, 129.2, 134.0, 138.0, 144.7, 153.2, 157.1, 170.7, 172.0 and 175.0 ppm; and/or (iv) an x-ray powder diffraction (XRPD) pattern which gives calcd. lattice spacings of 6.46, 5.39, 4.83, 4.68, 3.71, 3.63, 3.58, and 3.48 Angstroms; a process for prep. such a compd., a pharmaceutical compn. contg. such a compd. and the use of such a compd. in medicine.

IT 168553-12-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidiabetic action of polymorphic form of [(N-methyl-N-(pyridyl)amino)ethoxy]benzyl]thiazolidinedione maleate)

RN 168553-12-6 HCAPLUS

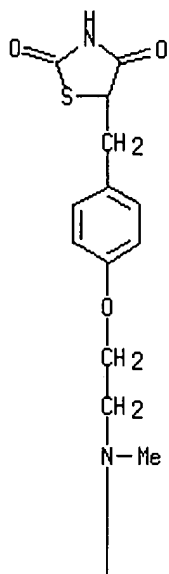
CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

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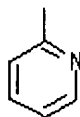
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CMF C18 H19 N3 O3 S

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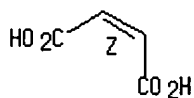
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CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

Double bond geometry as shown.



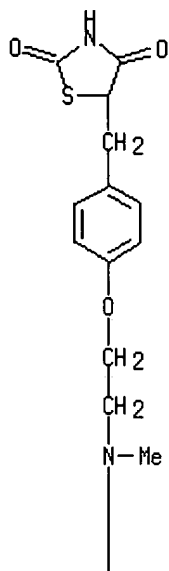
L8 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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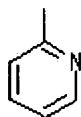
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DOCUMENT NUMBER: 133:340313
TITLE: Therapeutic action and properties of a polymorphic form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt
INVENTOR(S): Blackler, Paul David James; Giles, Robert Gordon; Sasse, Michael John
PATENT ASSIGNEE(S): SmithKline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064892	A2	20001102	WO 2000-GB1514	20000419
WO 2000064892	A3	20010125		
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NO 2001005149	A	20011217	NO 2001-5149	20011022
PRIORITY APPLN. INFO.:				
			GB 1999-9472	A 19990423
			GB 1999-12197	A 19990525
			WO 2000-GB1514	W 20000419
AB	A polymorphic form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt (the " Polymorph ") characterized in that it: (i) provides an IR spectrum contg. peaks at 1360, 1326, 1241, 714 and 669 cm ⁻¹ ; and/or (ii) provides a Raman spectrum contg. peaks at 1581, 768, 670, 271 and 226 cm ⁻¹ ; and/or (iii) provides a solid-state NMR spectrum contg. peaks at chem. shifts substantially; and/or (iv) provides an x-ray powder diffraction (XRPD) pattern contg. peaks; a process for prepg. such a compd., a pharmaceutical compn. contg. such a compd. and the use of such a compd. in medicine.			
IT	168553-12-6 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antidiabetic action of polymorphic form of [(N-methyl-N-(pyridyl)amino)ethoxy]benzyl]thiazolidinedione maleate)			
RN	168553-12-6 HCAPLUS			
CN	2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)			
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CMF	C18 H19 N3 O3 S			

PAGE 1-A



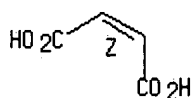
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CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

Double bond geometry as shown.



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FILE 'REGISTRY' ENTERED AT 19:34:58 ON 08 SEP 2002

L1 STRUCTURE UPLOADED

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L3 49 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 19:42:19 ON 08 SEP 2002

L4 477 S L3

L5 153 S L4 AND PD < JUNE 1999

L6 0 S L5 AND BLACKER, P?/AU

L7 0 S L4 AND BLACKIER, P?/AU

L8 3 S L4 AND POLYMORPH

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L5 ANSWER 1 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Citing
Text References

ACCESSION NUMBER: 2000:362595 HCAPLUS
DOCUMENT NUMBER: 133:13403
TITLE: Adipocyte containing ob gene promoter for screening modulators useful in treatment of anorexia, obesity, and other diseases
INVENTOR(S): Briggs, Michael R.; Auwerx, Johan; De Vos, Piet; Staels, Bart; Croston, Glenn E.; Miller, Stephen G.
PATENT ASSIGNEE(S): Ligand Pharmaceuticals Inc., USA
SOURCE: U.S., 64 pp., Cont.-in-part of U.S. Ser. No. 558,588, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6068976	A	20000530	US 1996-618100	19960319
CA 2215387	AA	19960926	CA 1996-2215387	19960319
PRIORITY APPLN. INFO.:				
			US 1995-408584	B2 19950320
			US 1995-418096	B2 19950405
			US 1995-510584	B2 19950802
			US 1995-558588	B2 19951030
			US 1995-7390P	P 19951121
			US 1995-7721P	P 19951130
			US 1995-8601P	P 19951214

AB This invention relates to the isolation and cloning of the promoter and other control regions of a human ob gene. It provides a method for identifying and screening for agents useful for the treatment of diseases and pathol. conditions affected by the level of expression of an ob gene. These agents interact directly or indirectly with the promoter or other control regions of the ob gene. A PPAR γ agonist, BRL49653, has been identified to be useful in treating anorexia, cachexia, and other diseases characterized by insufficient food intake or body wt. loss. Modulators of ob gene expression may be used to treat other diseases such as obesity, diabetes, hypertension, cardiovascular diseases and infertility.

IT **122320-73-4**, BRL49653

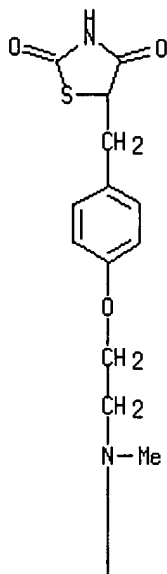
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(PPAR γ agonist; adipocyte contg. ob gene promoter for screening modulators useful in treatment of anorexia, obesity, and other diseases)

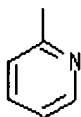
RN **122320-73-4** HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 2000:219115 HCAPLUS
 DOCUMENT NUMBER: 132:231972
 TITLE: Use of thiazolidinedione derivatives in the treatment of insulin resistance
 INVENTOR(S): Antonucci, Tammy; Lockwood, Dean; Norris, Rebecca
 PATENT ASSIGNEE(S): Warner-Lambert Company, USA
 SOURCE: U.S., 15 pp., Cont.-in-part of U.S. Ser. No. 124,707.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 7
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6046202	A	20000404	US 1998-168515	19981008
<u>US 5457109</u>	A	19951010	<u>US 1994-292585</u>	19940823
<u>US 5602133</u>	A	19970211	<u>US 1995-469398</u>	19950606
US 6046222	A	20000404	US 1997-868608	19970604
US 5972944	A	19991026	US 1998-124707	19980729
<u>AU 9952576</u>	A1	19991202	<u>AU 1999-52576</u>	19991001
PRIORITY APPLN. INFO.:			US 1993-122251	B2 19930915
			US 1994-292585	A3 19940823
			US 1995-469398	A2 19950606
			US 1996-763286	B2 19961210
			US 1997-856987	A2 19970515
			US 1997-868608	A3 19970604

US 1998-124707 A2 19980729
 AU 1997-17709 A3 19970403

OTHER SOURCE(S): MARPAT 132:231972

AB The invention provides methods of using a thiazolidinedione in the treatment of insulin resistance.

IT **122320-73-4**, Rosiglitazone

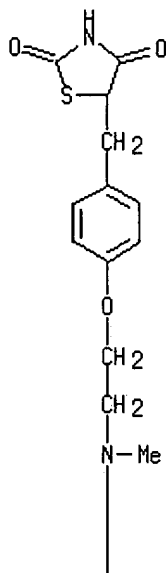
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(thiazolidinedione derivs. for treatment of insulin resistance)

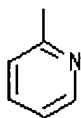
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 2000:29169 HCAPLUS
 DOCUMENT NUMBER: 132:288259
 TITLE: Rosiglitazone has no clinically significant effect on nifedipine pharmacokinetics
 AUTHOR(S): Harris, Robert Z.; Inglis, Anne Marie L.; Miller, Ann K.; Thompson, Kathleen A.; Finnerty, Dana; Patterson, Scott; Jorkasky, Diane K.; Freed, Martin I.
 CORPORATE SOURCE: Drug Metabolism and Pharmacokinetics, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
 SOURCE: Journal of Clinical Pharmacology (1999), 39(11), 1189-1194

CODEN: JCPCBR; ISSN: 0091-2700

PUBLISHER: Sage Publications
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To examine the effects of repeat oral dosing of rosiglitazone on the pharmacokinetics of nifedipine, a prototype CYP3A4 substrate, a randomized, open-label, crossover study was performed with two treatment phases sepd. by a washout period of at least 14 days. Twenty-eight healthy male volunteers received either a single 20 mg oral nifedipine dose or rosiglitazone 8 mg orally once daily for 14 days with a single 20 mg oral nifedipine dose administered on day 14. Plasma nifedipine concns. were detd. over the 24-h period following administration of the nifedipine doses. Lack of effect was defined as the demonstration that the 90% CI was contained entirely within a sym. 30% range either side of unity on the loge-scale. Following rosiglitazone + nifedipine administration, the area under the nifedipine concn.-time curve from time zero to infinity ($AUC(0-\infty)$) was 13% lower than that after administration of nifedipine alone. This difference in nifedipine $AUC(0-\infty)$ was not deemed to be clin. significant since the 90% CI was contained within the protocol-defined 30% range (point est. for ratio of geometric means 0.87; 90% CI: 0.79, 0.96). Rosiglitazone had no marked effect on nifedipine peak plasma concn. (point est.: 0.99; 90% CI: 0.73, 1.34) or time to peak concn. compared with nifedipine alone. Rosiglitazone coadministration produced a small decrease in the mean nifedipine half-life (point est.: -0.77; 90% CI: mean difference -1.29 h, -0.25 h). Both treatment regimens were well tolerated and assocd. with a favorable safety profile. Rosiglitazone, at the highest dose used in clin. studies, produced a small, clin. insignificant decrease in nifedipine exposure. The very small effect on nifedipine pharmacokinetics suggests that rosiglitazone is an extremely weak inducer of CYP3A4, a characteristic that distinguishes rosiglitazone from troglitazone.

IT **122320-73-4**, Rosiglitazone

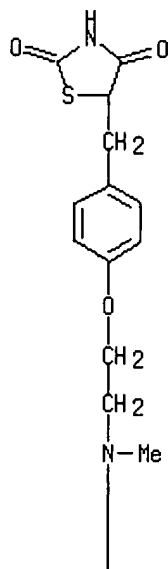
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(rosiglitazone effect on nifedipine pharmacokinetics)

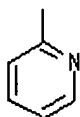
RN **122320-73-4** HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 2000:10630 HCAPLUS
DOCUMENT NUMBER: 132:44986
TITLE: Combinations of glitazones, biguanides, and optional sulfonylureas for treatment of diabetes
INVENTOR(S): Whitcomb, Randall Wayne
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. 5,859,037.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6011049	A	20000104	US 1998-189132	19981109
US 5859037	A	19990112	US 1997-970057	19971113
WO 2000027401	A1	20000518	WO 1999-US18140	19990811
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9953473	A1	20000529	AU 1999-53473	19990811
EP 1128834	A1	20010905	EP 1999-939130	19990811
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:

US 1997-38224P	P	19970219
US 1997-970057	A2	19971113
US 1998-189132	A	19981109
WO 1999-US18140	W	19990811

AB Combinations of a glitazone antidiabetic agent and a biguanide antidiabetic agent, and optionally a sulfonylurea antidiabetic agent, are useful for treating diabetes mellitus and improving glycemic control.

IT **122320-73-4**, Rosiglitazone

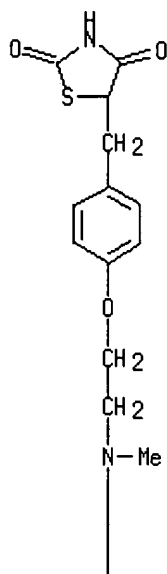
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combinations of glitazones, biguanides, and optional sulfonylureas for diabetes treatment)

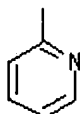
RN **122320-73-4** HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1999:810151 HCAPLUS
DOCUMENT NUMBER: 132:102683
TITLE: Therapeutic index for rosiglitazone in dietary obese rats: separation of efficacy and hemodilution
AUTHOR(S): Pickavance, L. C.; Tadayyon, M.; Widdowson, P. S.; Buckingham, R. E.; Wilding, J. P. H.
CORPORATE SOURCE: Department of Medicine, University of Liverpool, Liverpool, L69 3GA, UK
SOURCE: British Journal of Pharmacology (1999), 128(7), 1570-1576
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The blood glucose-lowering efficacy of rosiglitazone (RSG) and the mechanisms of assocd. wt. gain were detd. in dietary obese rats (DIOs). DIO and chow-fed rats received RSG 0.3-30 mg kg⁻¹ daily for 21 days. In DIOs, plasma glucose and insulin concns. were reduced by RSG at dosages of 3 and 10 mg kg⁻¹, resp. Homeostasis model assessment (HOMA) indicated the threshold for a redn. of insulin resistance was 1 mg kg⁻¹. Neither glucose nor insulin levels were affected by treatment in chow-fed rats. RSG 0.3 mg kg⁻¹ lowered free fatty acids (FFAs) in DIOs, whereas for plasma triglycerides (TGs), the threshold was 3 mg kg⁻¹. By contrast, the threshold for reducing packed red cell vol. (PCV) and increasing cardiac mass was 10 mg kg⁻¹. Thus, the therapeutic index for RSG in DIOs was >3 and ≤10. Energy intake and wt. gain increased in treated DIOs (by 20% and 50 g, at 30 mg kg⁻¹) and chow-fed rats (by 25% and 35 g, at 30 mg

kg-1). In DIOs, these increases coincided with falls in plasma leptin (40% lower at 30 mg kg-1) and insulin (43% lower at 30 mg kg-1). By contrast, in chow-fed rats, wt. gain and hyperphagia occurred without changes in either leptin or insulin. However, redns. in FFAs below 0.4-0.3 mM were assocd. with hyperphagia and wt. gain in DIO and chow-fed rats. We conclude that increased energy intake and body wt. did not attenuate the improved metab. evoked by RSG in DIO rats, and that insulin action was enhanced at a dose >3 fold below the threshold for causing hemodilution and cardiac hypertrophy in DIO rats.

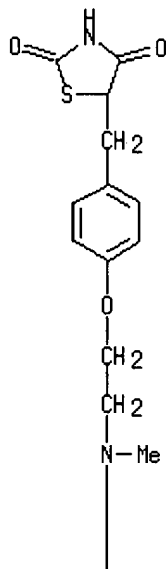
IT **122320-73-4**, Rosiglitazone

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic index for rosiglitazone in dietary obese rats)

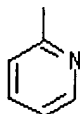
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'REGISTRY' ENTERED AT 19:34:58 ON 08 SEP 2002

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L2 2 S L1

L3 49 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 19:42:19 ON 08 SEP 2002

L4 477 S L3
L5 153 S L4 AND PD < JUNE 1999
L6 0 S L5 AND BLACKER, P?/AU
L7 0 S L4 AND BLACKIER, P?/AU
L8 3 S L4 AND POLYMORPH

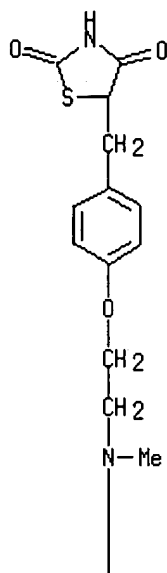
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L5 ANSWER 6 OF 153 HCAPLUS COPYRIGHT 2002 ACS

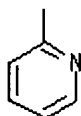
Full Text	Citing References
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ACCESSION NUMBER: 1999:807214 HCAPLUS
DOCUMENT NUMBER: 132:146491
TITLE: Differential block by troglitazone and rosiglitazone of glibenclamide-sensitive K⁺ current in rat aorta myocytes
AUTHOR(S): Mishra, S. K.; Aaronson, P. I.
CORPORATE SOURCE: St Thomas's Campus, The Guy's, Department of Pharmacology, King's College and St Thomas' Hospitals' Medical and Dental School, London, UK
SOURCE: European Journal of Pharmacology (1999), 386(1), 121-125
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thiazolidinediones are insulin-sensitizing agents effective in controlling type II diabetes. These compds. also cause vasodilation. We evaluated the effects of the thiazolidinediones troglitazone and rosiglitazone on the glibenclamide-sensitive K⁺ current in freshly isolated rat aorta myocytes. Troglitazone inhibited this current in a concn.-dependent manner (IC₅₀~1 µM). Rosiglitazone had a similar, but much less potent (IC₅₀~20 µM) action. Block of the glibenclamide-sensitive K⁺ channels, in particular by troglitazone, may potentially affect the response of arteries to hypoxia and to certain endogenous and exogenous vasodilators.
IT **122320-73-4**, Rosiglitazone
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (differential block by troglitazone and rosiglitazone of glibenclamide-sensitive K⁺ current in aorta myocytes)
RN 122320-73-4 HCAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1999:799229 HCAPLUS
 DOCUMENT NUMBER: 132:88016
 TITLE: Studies on the euglycemic and hypolipidemic potentials of the novel indole analogue of thiazolidinedione, DRF 2189
 AUTHOR(S): Chakrabarti, Ranjan; Vikramadithyan, Reeba Kannimel; Dileepkumar, Tripuraneni; Kumar, Kochunarayanapillai Bhadrappa Sunil; Kumar, Mamnoor Prem; Misra, Parimal; Rao, Paraselli Bheema; Lohray, Vidya Bhusan; Lohray, Braj Bhusan; Rajagopalan, Ramanujam
 CORPORATE SOURCE: Department of Pharmacology, Dr. Reddy's Research Foundation, Hyderabad, India
 SOURCE: Arzneimittelforschung (1999), 49(11), 905-911
 CODEN: ARZNAD; ISSN: 0004-4172
 PUBLISHER: Editio Cantor Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Euglycemic and hypolipidemic activities of a novel indole analog of thiazolidinedione, DRF 2189 (CAS 172647-53-9), have been evaluated in different animal models. Compared to troglitazone (CAS 97322-87-7), DRF 2189 exhibited interesting plasma glucose and triglyceride lowering activity in genetically diabetic and obese db/db mice. It also produced a significant redn. in plasma glucose, triglyceride, total cholesterol levels and improvement in oral glucose tolerance in another genetic mouse model, the ob/ob mice. In high-fat diet fed Sprague-Dawley rats, DRF 2189 treatment showed improvement in plasma lipid parameters. Like other thiazolidinediones, this compd. also possesses peroxisome proliferator

activated receptor gamma (PPAR γ) transactivation potential. In anesthetized rat expt., DRF 2189 produced a transient fall in blood pressure without any change in the ECG pattern. It showed non-specific smooth muscle relaxant activity against acetylcholine-, histamine- and potassium chloride-induced contractions in isolated guinea pig ileum. A twenty-eight-day toxicity study in Wistar rats did not show any signs of treatment-related adverse effects. The overall antidiabetic and hypolipidemic activities of DRF 2189 are comparable with rosiglitazone (CAS 155141-29-0) and superior to troglitazone. In conclusion, results from these preclin. studies indicate that DRF 2189, a novel thiazolidinedione, has a marked potential for the management of type-2 diabetes.

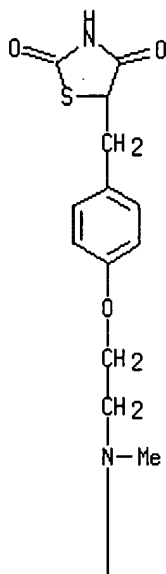
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 153 HCAPLUS COPYRIGHT 2002 ACS

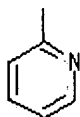
Full Text	Citing References
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ACCESSION NUMBER: 1999:792188 HCAPLUS
DOCUMENT NUMBER: 132:18391
TITLE: Thiazolidinediones in the treatment of insulin resistance syndrome
AUTHOR(S): Cawthorne, M. A.
CORPORATE SOURCE: Clore Laboratory, University of Buckingham, Buckingham, MK18 1EG, UK
SOURCE: Progress in Obesity Research (1999), 8, 517-524
CODEN: POBREJ; ISSN: 0962-7936
PUBLISHER: John Libbey & Co. Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 14 refs. This article discusses the insulin sensitizing actions of thiazolidinediones, their mechanism of action, and preclin. and clin. effects in diabetes treatment.
IT 122320-73-4, Rosiglitazone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thiazolidinediones in treatment of insulin resistance syndrome in humans)
RN 122320-73-4 HCAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 1999:789202 HCAPLUS
DOCUMENT NUMBER: 132:117393
TITLE: Chronic and acute effects of thiazolidinediones BM13.1258 and BM15.2054 on rat skeletal muscle glucose metabolism
AUTHOR(S): Furnsinn, C.; Brunmair, B.; Meyer, M.; Neschen, S.; Furtmuller, R.; Roden, M.; Kuhnle, H. F.; Nowotny, P.; Schneider, B.; Waldhausl, W.
CORPORATE SOURCE: Division of Endocrinology & Metabolism, Department of Medicine III, Vienna, A-1090, Austria
SOURCE: British Journal of Pharmacology (1999), 128(6), 1141-1148
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1 New thiazolidinediones BM13.1258 and BM15.2054 were studied with regard to their PPAR γ -agonistic activities and to their acute and chronic effects on glucose metab. in soleus muscle strips from lean and genetically obese rats. 2 Both BM13.1258 and BM15.2054 revealed to be potent PPAR γ -activators in transient transfection assays in vitro. 3 In insulin-resistant obese rats, but not in lean rats, 10 days of oral treatment with either compd. increased the stimulatory effect of insulin on muscle glycogen synthesis to a similar extent (insulin-induced increment in μ mol glucose incorporated into glycogen g⁻¹ h⁻¹: control, +1.19 \pm 0.28; BM13.1258, +2.50 \pm 0.20; BM15.2054, +2.55 \pm 0.46; P<0.05 vs control each). 4 In parallel to insulin sensitization, mean glucose

oxidn. increased insulin independently in response to BM13.1258 (to 191 and 183% of control in the absence and presence of insulin, resp.; $P < 0.01$ each), which was hardly seen in response to BM15.2054 (to 137 and 124% of control, resp.; ns). 5 Comparable effects on PPAR γ activation and on amelioration of insulin resistance by BM13.1258 and BM15.2054 were therefore opposed by different effects on glucose oxidn. 6 In contrast to chronic oral treatment, acute exposure of muscles to BM13.1258 or BM15.2054 in vitro elicited a distinct catabolic response of glucose metab. in specimens from both lean and obese rats. 7 The results provide evidence that BM13.1258 and BM15.2054 can affect muscle glucose metab. via more than one mechanism of action. 8 Further efforts are required to clarify, to what extent other mechanisms besides insulin sensitization via the activation of PPAR γ are involved in the antidiabetic actions of thiazolidinediones.

IT **122320-73-4**, Rosiglitazone

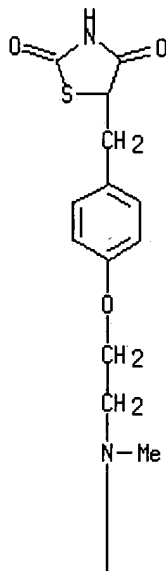
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(thiazolidinediones BM13.1258 and BM15.2054 chronic and acute effects on skeletal muscle glucose metab.)

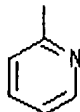
RN **122320-73-4** HCAPLUS

CN **2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)**

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REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1999:724649 HCAPLUS
DOCUMENT NUMBER: 132:202442

TITLE: Rosiglitazone: a new agent of the thiazolidinedione class for treatment of the type 2 diabetic patient
 AUTHOR(S): Amato, Paul V.; Domenichini, David
 CORPORATE SOURCE: Hartford Hospital, Hartford, CT, USA
 SOURCE: Formulary (1999), 34(10), 825-826, 829-830, 832, 835
 CODEN: FORMF9; ISSN: 1082-801X
 PUBLISHER: Advanstar Communications, Inc.
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review with 33 refs. Rosiglitazone is an orally active antidiabetic agent of the thiazolidinedione class. It was approved by the FDA in May, 1999, as monotherapy and in combination with metformin for the treatment of type 2 diabetic patients. As a potent agonist of peroxisome proliferator-activated receptor γ , rosiglitazone is theorized to improve glycemic control by improving insulin sensitivity in adipose tissue, skeletal muscle, and liver. Clin. trials of rosiglitazone as monotherapy and in combination with metformin, sulfonylureas, or insulin have shown clin. and significant effects on HbA1c and fasting blood glucose. The most common adverse effects have been respiratory tract infections, injury, and headache. Clin. data show no evidence of hepatotoxicity or elevations in liver enzymes. The usual starting dosage is 4 mg/day given once daily or in two divided doses; this dosage may be increased to 8 mg/day. Rosiglitazone appears to be an effective, safe, and competitively priced agent for the treatment of type 2 diabetics.

IT 122320-73-4, Rosiglitazone

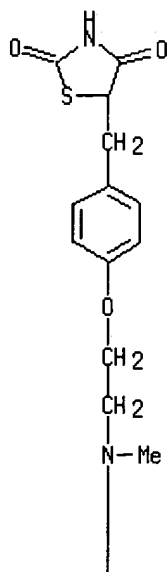
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(rosiglitazone: a new agent of the thiazolidinedione class for treatment of human type 2 diabetes)

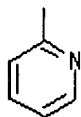
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1999:704526 HCAPLUS
 DOCUMENT NUMBER: 132:59006
 TITLE: Regulation of gene expression by activation of the peroxisome proliferator-activated receptor γ with rosiglitazone (BRL 49653) in human adipocytes
 AUTHOR(S): Rieusset, Jennifer; Auwerx, Johan; Vidal, Hubert
 CORPORATE SOURCE: Faculte de Medecine Rene Laennec, INSERM U449, Universite Claude Bernard Lyon-1, Lyon, 69372, Fr.
 SOURCE: Biochemical and Biophysical Research Communications (1999), 265(1), 265-271
 CODEN: BBRCA9; ISSN: 0006-291X
 PUBLISHER: Academic Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB To better define the mechanism of action of the thiazolidinediones, we incubated freshly isolated human adipocytes with rosiglitazone and investigated the changes in mRNA expression of genes encoding key proteins of adipose tissue functions. Rosiglitazone (10⁻⁶ M, 4 h) increased p85 α phosphatidylinositol 3-kinase (p85 α PI-3K) and uncoupling protein-2 mRNA levels and decreased leptin expression. The mRNA levels of insulin receptor, IRS-1, Glut 4, lipoprotein lipase, hormone-sensitive lipase, acylation-stimulating protein, fatty acid transport protein-1, angiotensinogen, plasminogen activator inhibitor-1, and PPAR γ 1 and γ 2 were not modified by rosiglitazone treatment. Activation of RXR, the partner of PPAR γ , in the presence of rosiglitazone, increased further p85 α PI-3K and UCP2 mRNA levels and produced a significant augmentation of Glut 4 expression. Because p85 α PI-3K is a major component of insulin action, the induction of its expression might explain, at least in part, the insulin-sensitizing effect of the thiazolidinediones. (c) 1999 Academic Press.

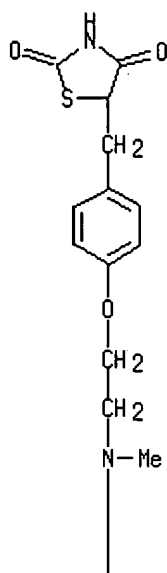
IT 122320-73-4, Rosiglitazone

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (gene expression of proteins involved in adipose tissue metab. as mechanism of PPAR γ -selective antidiabetic rosiglitazone in human adipocytes)

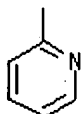
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 19:34:46 ON 08 SEP 2002)

FILE 'REGISTRY' ENTERED AT 19:34:58 ON 08 SEP 2002

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L2 2 S L1
L3 49 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 19:42:19 ON 08 SEP 2002

L4 477 S L3
L5 153 S L4 AND PD < JUNE 1999
L6 0 S L5 AND BLACKER, P?/AU
L7 0 S L4 AND BLACKIER, P?/AU
L8 3 S L4 AND POLYMORPH

=> d 15, ibib abs fhitstr, 20-25

L5 ANSWER 20 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER:	1999:617848 HCAPLUS
DOCUMENT NUMBER:	132:117298
TITLE:	Peroxisome proliferator-activated receptor activators target human endothelial cells to inhibit leukocyte-endothelial cell interaction
AUTHOR(S):	Jackson, Simon M.; Parhami, Farhad; Xi, Xiao-Ping; Berliner, Judith A.; Hsueh, Willa A.; Law, Ronald E.; Demer, Linda L.

CORPORATE SOURCE: Department of Medicine, University of California, Los Angeles, School of Medicine, Los Angeles, CA, 90095-1679, USA

SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology (1999), 19(9), 2094-2104
CODEN: ATVBFA; ISSN: 1079-5642

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An early event in acute and chronic inflammation and assocd. diseases such as atherosclerosis and rheumatoid arthritis is the induced expression of specific adhesion mols. on the surface of endothelial cells (ECs), which subsequently bind leukocytes. Peroxisome proliferator-activated receptors (PPARs), members of the nuclear receptor superfamily of transcription factors, are activated by fatty acid metabolites, peroxisome proliferators, and thiazolidinediones and are now recognized as important mediators in the inflammatory response. Whether PPAR activators influence the inflammatory responses of ECs is unknown. The authors show that the PPAR activators 15-deoxy- Δ 12,14-prostaglandin J2 (15d-PGJ2), Wyeth 14643, ciglitazone, and troglitazone, but not BRL 49653, partially inhibit the induced expression of vascular cell adhesion mol.-1 (VCAM-1), as measured by ELISA, and monocyte binding to human aortic endothelial cells (HAECs) activated by phorbol 12-myristate 13-acetate (PMA) or lipopolysaccharide. The "natural" PPAR activator 15d-PGJ2 had the greatest potency and was the only tested mol. capable of partially inhibiting the induced expression of E-selectin and neutrophil-like HL60 cell binding to PMA-activated HAECs. Intracellular adhesion mol.-1 induction by PMA was unaffected by any of the mols. tested. Both PPAR- α and PPAR- γ mRNAs were detected in HAECs by using reverse transcription-polymerase chain reaction and a RNase protection assay; however, the authors have yet to det. which, if any, of the PPARs are mediating this process. Certain PPAR activators may thus help limit chronic inflammation mediated by VCAM-1 and monocytes without affecting acute inflammation mediated by E-selectin and neutrophil binding.

IT 122320-73-4, BRL 49653

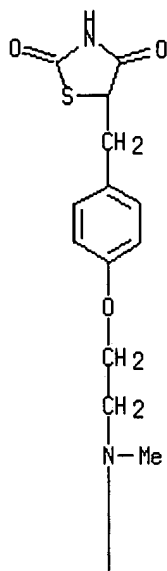
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peroxisome proliferator-activated receptor activators target human endothelial cells to inhibit leukocyte-endothelial cell interaction)

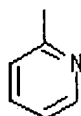
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 1999:607181 HCAPLUS
DOCUMENT NUMBER: 131:237812
TITLE: Cell culture conditions determine apolipoprotein CIII secretion and regulation by fibrates in human hepatoma HepG2 cells
AUTHOR(S): Clavey, Veronique; Copin, C.; Mariotte, M. C.; Bauge, E.; Chinetti, G.; Fruchart, J.; Fruchart, J. C.; Dallongeville, J.; Staels, B.
CORPORATE SOURCE: Faculte Pharmacie, Univ. Lille 2, Lille, Fr.
SOURCE: Cellular Physiology and Biochemistry (1999), 9(3), 139-149
CODEN: CEPBEW; ISSN: 1015-8987
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fibrates are widely used drugs which lower triglycerides and increase HDL concns. in blood serum. Recent findings from our lab. have shown that fibrates repress apolipoprotein (apo) CIII gene expression, an effect that explains partially the triglyceride-lowering activity of these drugs. The effect of various fibrates on apo CIII gene expression in the human hepatoblastoma cell line HepG2 was studied. The authors demonstrate that the level of apo CIII secretion by HepG2 cells is controlled by serum factors whereas apo CIII mRNA levels are not and even increase under conditions when apo CIII secretion dramatically decreases. 12 Fetal calf serum batches were tested and apo CIII secretion in cell medium was only detected with 3 of them. The effect of serum on apolipoprotein secretion was more pronounced for apo CIII whereas other apolipoproteins (apo E, apo

B, apo AII and apo AI) were affected to a lesser extent. Under serum conditions allowing apo CIII secretion, treatment with the peroxisome-proliferator activated receptor (PPAR) α activators fenofibrate, gemfibrozil and Wy-14643 result in a marked lowering of apo CIII secretion and gene expression, this effect being most pronounced with Wy-14643. Comparison of the activity of a PPAR γ -specific ligand, the antidiabetic thiazolidinedione, BRL-49653 and a PPAR α ligand Wy-14643 showed a marked decrease of apo CIII secretion and gene expression after activation of PPAR α but not PPAR γ . In conclusion, fibrates down-regulate apo CIII gene expression in human HepG2 cells, most likely via PPAR α but not via PPAR γ . However, these effects are only obsd. in HepG2 cells cultured under appropriate conditions.

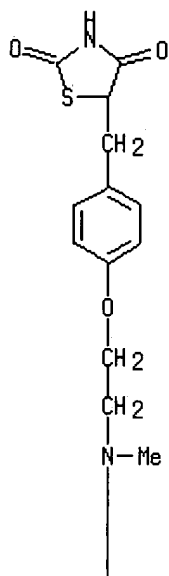
IT **122320-73-4**, BRL-49653

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antidiabetic effect on apolipoprotein secretion and regulation by fibrates in hepatoma HepG2 cells)

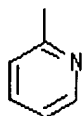
RN **122320-73-4** HCAPLUS

CN **2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)**

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REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 22 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 1999:590400 HCAPLUS
DOCUMENT NUMBER: 132:121278
TITLE: Use of a PPAR gamma-specific monoclonal antibody to

demonstrate thiazolidinediones induce PPAR gamma
 receptor expression in vitro
 AUTHOR(S): Su, Jui-Lan; Winegar, Deborah A.; Wisely, G. Bruce;
 Sigel, Carlisle S.; Hull-Ryde, Emily A.
 CORPORATE SOURCE: Department of Molecular Sciences, Glaxo Wellcome
 Research and Development, Research Triangle Park, NC,
 27709, USA
 SOURCE: Hybridoma (1999), 18(3), 273-280
 CODEN: HYBRDY; ISSN: 0272-457X
 PUBLISHER: Mary Ann Liebert, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Troglitazone and rosiglitazone (BRL49653), members of the
 thiazolidinedione (TZD) class of antidiabetic drugs, are peroxisome
 proliferator-activated receptor γ (PPAR γ) ligands that induce
 adipocyte differentiation and increase the expression of PPAR γ
 protein. Here, we report the characterization of a PPAR γ specific
 monoclonal antibody (MAb), PyA53.25, and its use to monitor
 PPAR γ expression in the noncommitted pluripotent murine mesenchymal
 stem cell line, C3H10T1/2, treated with TZDs. MAb PyA53.25 was
 raised against a region in the N-terminal domain of human PPAR γ
 shared by splice variants PPAR γ 1 and PPAR γ 2. It recognizes
 immunizing antigen in enzyme-linked immunoadsorbent assay (ELISA), and
 does not cross-react with the N-terminal domains of PPAR α or
 PPAR δ . In Western blotting, PyA53.25 reacts with the
 immunizing antigen as well as distinct protein bands corresponding to the
 mol. wt. of full length PPAR γ from C3H10T1/2 cells and rat tissue
 lysates. In fluorescent microscopy, PyA53.25 immunostains nuclei of
 C3H10T1/2 cells treated with PPAR γ ligands. The fluorescence
 intensity of the treated cells is TZD dose-dependent, and correlates with
 lipid accumulation consistent with adipogenesis. Based on these results,
 we propose that MAb PyA53.25 will be a useful tool for elucidating
 the role of PPAR γ in fatty acid metab. and adipocyte
 differentiation.

IT 122320-73-4, Rosiglitazone

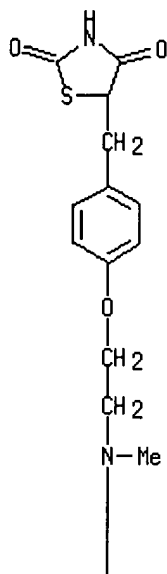
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)

(use of a PPAR gamma-specific monoclonal antibody to demonstrate
 thiazolidinediones induce PPAR gamma receptor expression in mesenchymal
 stem cells)

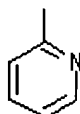
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met
 hyl]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 23 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1999:533775 HCAPLUS
 DOCUMENT NUMBER: 131:266844
 TITLE: A novel therapy for colitis utilizing PPAR- γ ligands to inhibit the epithelial inflammatory response
 AUTHOR(S): Su, Chinyu G.; Wen, Xiaoming; Bailey, Shannon T.; Jiang, Wen; Rangwala, Shamina M.; Keilbaugh, Sue A.; Flanigan, Anne; Murthy, Sreekant; Lazar, Mitchell A.; Wu, Gary D.
 CORPORATE SOURCE: Division of Gastroenterology, University of Pennsylvania School of Medicine, Philadelphia, PA, 19104, USA
 SOURCE: Journal of Clinical Investigation (1999), 104(4), 383-389
 CODEN: JCINAO; ISSN: 0021-9738
 PUBLISHER: American Society for Clinical Investigation
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Peroxisome proliferator-activated receptor γ (PPAR- γ), a member of the nuclear hormone receptor super-family originally shown to play a crit. role in adipocyte differentiation and glucose homeostasis, has recently been implicated as a regulator of cellular proliferation and inflammatory responses. Colonic epithelial cells, which express high levels of PPAR- γ protein, have the ability to produce inflammatory cytokines that may play a role in inflammatory bowel disease (IBD). We report here that PPAR- γ ligands dramatically attenuate cytokine gene

expression in colon cancer cell lines by inhibiting the activation of nuclear factor- κ B via an I κ B- α -dependent mechanism. Moreover, thiazolidinedione ligands for PPAR- γ markedly reduce colonic inflammation in a mouse model of IBD. These results suggest that colonic PPAR- γ may be a therapeutic target in humans suffering from IBD.

IT 122320-73-4, BRL 49653

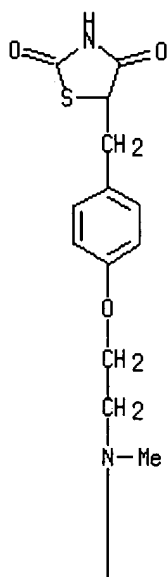
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(a novel therapy for colitis utilizing PPAR- γ ligands to inhibit the epithelial inflammatory response)

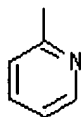
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 24 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1999:467127 HCAPLUS

DOCUMENT NUMBER: 131:237802

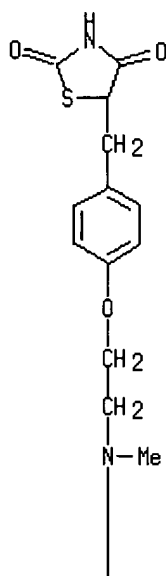
TITLE: Novel euglycemic and hypolipidemic agents: pyridine containing unsaturated thiazolidinediones

AUTHOR(S): Lohray, B. B.; Bhushan, Vidya; Reddy, A. Sekar; Rao, P. Bheema; Reddy, N. Jaipal; Reddy, K. Anantha; Vikramadithyan, Reeba K.; Rajagopalan, R.

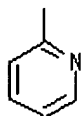
CORPORATE SOURCE: Department of Medicinal Chemistry and Drug Discovery, Dr. Reddy's Research Foundation, Hyderabad, 500 050,

SOURCE: India
 Indian Journal of Chemistry, Section B: Organic
 Chemistry Including Medicinal Chemistry (1999),
 38B(4), 403-406
 CODEN: IJSBDB; ISSN: 0376-4699
 PUBLISHER: National Institute of Science Communication, CSIR
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Pyridyl contg. 2,4-thiazolidinediones having cyclic amine as linker have
 been synthesized. Both unsatd. thiazolidinedione 6 and satd.
 thiazolidinedione 5 and their various salts have been evaluated in db/db
 mice for euglycemic and hypolipidemic effects. The maleate salt of TZD 6a
 is found to be a very potent euglycemic and hypolipidemic compd.
 IT **122320-73-4P**, BRL 49653
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); SPN (Synthetic preparation); BIOL (Biological
 study); PREP (Preparation)
 (novel euglycemic and hypolipidemic agents: pyridine contg. unsatd.
 thiazolidinediones)
 RN **122320-73-4** HCAPLUS
 CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met
 hyl]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 25 OF 153 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1999:446177 HCAPLUS
 DOCUMENT NUMBER: 131:209060
 TITLE: Rosiglitazone (BRL49653), a PPAR γ -selective

agonist, causes peroxisome proliferator-like liver effects in obese mice
 AUTHOR(S): Edvardsson, Ulrika; Bergstrom, Monica; Alexandersson, Maria; Bamberg, Krister; Ljung, Bengt; Dahllof, Bjorn
 CORPORATE SOURCE: Cell Biology and Biochemistry, Astra Hassle AB, Moelndal, S-431 83, Swed.
 SOURCE: Journal of Lipid Research (1999), 40(7), 1177-1184
 CODEN: JLPRAW; ISSN: 0022-2275
 PUBLISHER: Lipid Research, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The PPAR (peroxisome proliferator activated receptor) transcription factors are ligand-activated nuclear receptors that regulate genes involved in lipid metab. and homeostasis. PPAR α is preferentially expressed in liver and PPAR γ preferentially in adipose tissue. Activation of PPAR α leads to peroxisome proliferation and increased β -oxidn. of fatty acids in rodents. PPAR γ -activation leads to adipocyte differentiation and improved insulin signaling of mature adipocytes. Both PPAR receptors are believed to be functional targets for treatment of hyperlipidemia in man. The authors have treated obese diabetic mice (ob/ob), which have highly elevated levels of plasma triglycerides, glucose and insulin, for 1 wk with WY14,643 (180 μ mol/kg/day), a selective PPAR α agonist, or rosiglitazone (BRL49653; 2.5 μ mol/kg/day), a selective PPAR γ agonist. The doses used produce a similar therapeutic effect in both treatment groups (lowering of triglycerides and glucose). High resolu. two-dimensional gel electrophoresis of livers showed that WY14,643 and rosiglitazone both produced changes in expression pattern of many proteins involved in peroxisomal fatty acid β -oxidn. However, similar expts. performed in lean mice showed significant up-regulation of these proteins only with WY14,643 treatment. Furthermore, the proteins up-regulated by the drugs in obese mice had a higher basal expression in obese controls compared to the lean littermates. Liver PPAR γ mRNA levels were detd. and the authors obsd. that PPAR γ 2 mRNA levels were elevated in obese mice compared to lean littermates. As PPAR α and PPAR γ recognize similar DNA response elements, it is likely that the effects of rosiglitazone on PPAR α responsive genes in livers of the ob/ob mice are mediated by PPAR γ 2.

IT 122320-73-4, Rosiglitazone

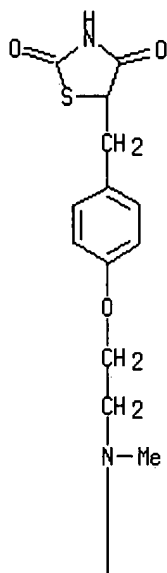
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(PPAR γ -selective agonist rosiglitazone (BRL49653) causes peroxisome proliferator-like liver effects in obese mice in relation to WY14,643 and hypolipemic and hypoglycemic effects)

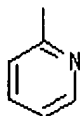
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
100.65	245.32

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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L3 49 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 19:42:19 ON 08 SEP 2002

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L5 153 S L4 AND PD < JUNE 1999
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L8 3 S L4 AND POLYMORPH

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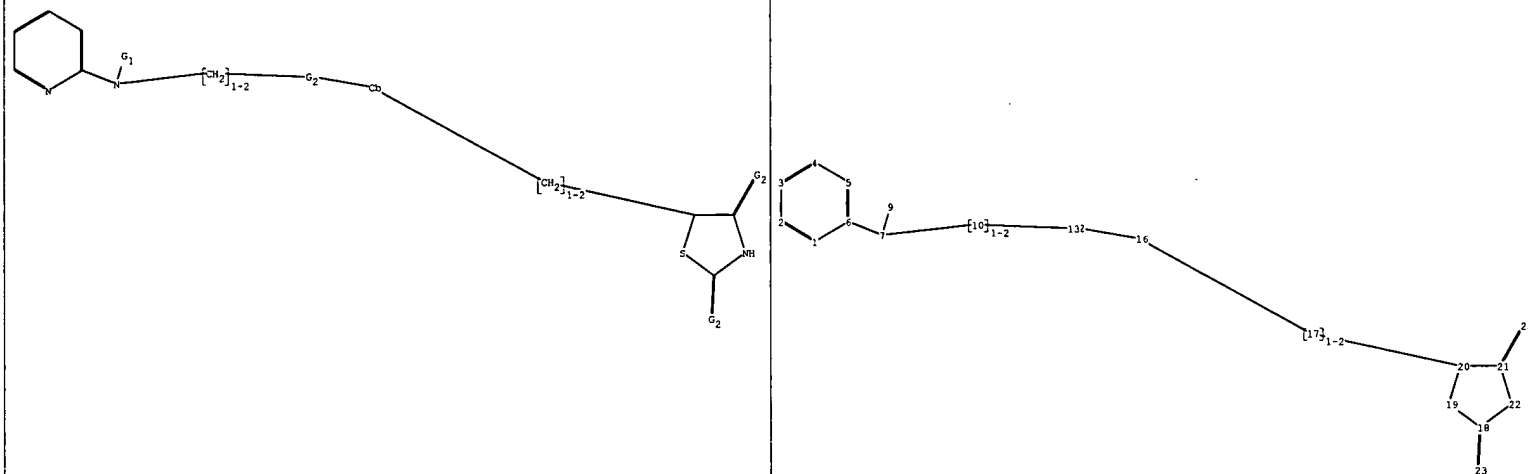
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	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-12.39

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(Untitled)



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ring nodes :

1 2 3 4 5 6 18 19 20 21 22

chain bonds :

6-7 7-9 7-10 10-13 12-16 16-17 17-20 18-23 21-25

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 18-19 18-22 19-20 20-21 21-22

exact/norm bonds :

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exact bonds :

7-10 10-13 16-17 17-20 18-19 19-20 20-21

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems :

containing 1 : 18 :

G1:CH3,Et

G2:O,S

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 9:CLASS 10:CLASS 12:CLASS
13:CLASS 16:Atom 17:CLASS 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:CLASS
25:CLASS

Generic attributes :

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Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Type of Ring System : Monocyclic

Element Count :

Node 16: Limited

C, C6